

## REMARKS

Claims 1-24 are pending in the application and claims 15-24 have been withdrawn from consideration. Applicants hereby cancel claims 15-24. Claims 5-7 and 12-14 have been amended. Support for the claim amendment "in any configuration that maintains the desired activity of said label and said moiety" can be found on page 25 (second full paragraph) and Figure 1. Support for the amendments to claims 4 and 11 may be found, for example, on page 18-19, and 29. Support for new claims 25-34 may be found, for example, on pages 4-5, 18-23, 35-37, 39, 42, Figures 3 through 8. No new matter has been added by the amendments.

Amendment or withdrawal of the pending claims should in no way be construed as an acquiescence, narrowing, or surrender of any subject matter. The amendments and withdrawals are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application. Applicants reserve the option to prosecute the pending claims further, or other ones, in the instant or a subsequent patent application.

## CLAIM REJECTIONS

### *Rejection of claims under 35 U.S.C. § 112, second paragraph*

The Examiner has rejected claims 4-7 and 11-14 as being indefinite. Specifically, the Examiner points out that claims 4 and 11 are rejected because “the metes and bounds of the term ‘analog’ cannot be determined”. In order to expedite prosecution and not in acquiescence to the rejections, Applicants have amended claims 4 and 11 to further define the term “analog”. Applicants submit that this amendment obviates the rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 5-7 and 12-14 have been rejected for being “unclear whether the various components (e.g. the targeting moiety, oligonucleotide and detectable label) listed in the corresponding claims are directly coupled to each other, or indirectly coupled to each other”. In order to expedite prosecution and not in acquiescence to the rejections, Applicants have amended claims 5-7 and 12-14 to recite “in any configuration that maintains the desired activity of said label and said moiety”. With respect to this amendment, Applicants believe that claims 5-7 and 12-14 are fully in accord with the support provided within the specification. Further, Applicants respectfully submit that the claim amendments made herein fully overcome and obviate the stated grounds for rejection of said claim. Applicants respectfully urge the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph.

### *Rejection of claims under 35 U.S.C. § 102(e) over Rothschild, et al.*

The Examiner has rejected claims 1-14 as being anticipated by Rothschild et al. (U.S. Patent No. 6,589,736). The Examiner alleges that Rothschild et al. teaches “conjugates comprising an oligonucleotide that targets to a sequence of interest (antisense sequences), a protein targeting moiety, a polypeptide therapeutic agent and a fluorescent or chemiluminescent detectable label, which targeting moiety localizes to a site in an organism, and wherein the targeting moiety, detectable label and nucleotide are optionally coupled covalently to each other”. Applicants respectfully traverse this rejection.

A claim is anticipated only if each and every element of the claim is found in a single prior art reference. The instant invention discloses a targeted oligonucleotide construct

comprising at least three components: (1) a targeting moiety which localizes to a site in an organism; (2) an oligonucleotide complementary to a nucleic acid of interest (see page 2, paragraph 6; page 5, paragraph 3; pages 18-23, page 44, paragraph 6; pages 45-47); and (3) a detectable label, which may be tethered in various configurations. Nowhere in the Rothschild reference is a conjugate having these three components described. Rather, the Rothschild reference teaches two-component conjugates having (1) a photocleavable group capable of covalently binding to a substrate, which photocleavable group is coupled, optionally via a tether to a (2) detectable moiety. The presently claimed invention does not contain a photocleavable group, and it contains instead two other components, a targeting moiety and an oligonucleotide complementary to a nucleic acid of interest. Further Thus, the Rothschild reference does not anticipate each and every element of claims 1-14. Applicants respectfully request reconsideration and withdrawal of the present rejection.

**Rejection of claims under 35 U.S.C. § 102(e) over Papahadjopoulos, et al.**

The Examiner has rejected claims 1-5, and 8-11 as being anticipated by Papahadjopoulos et al. (U.S. Patent No. 6,410,049). The Examiner alleges that Papahadjopoulos et al. teaches “conjugated complexes comprising an oligonucleotide that targets a sequence of interest (an antisense), a protein targeting moiety that localizes to a site in an organism, and optionally further comprising a chemiluminescent detectable label, wherein the oligonucleotide and the targeting moiety are coupled”.

Papahadjopoulos et al. discloses the use of a nucleic acid as a targeting moiety. This reference defines the term “targeting moiety” to refer to “all molecules capable of specifically binding to a particular target molecule and forming a bound complex as described above. Thus the ligand and its corresponding target molecule form a specific binding pair. Examples include, but are not limited to antibodies, lymphokines, cytokines, receptor proteins such as CD4 and CD8, solubilized receptor proteins such as soluble CD4, hormones, growth factors, and the like which specifically bind desired target cells, and nucleic acids which bind corresponding nucleic acids through base pair complementarity” (See Col 5, lines 58-67 and Col 6, lines 1-2).

In contrast, the instant invention contemplates targeting moieties that are “any molecular structure which assists the construct in localizing to a particular target area, entering a target

cell(s), and/or binding to a target receptor. For example, lipids (including cationic, neutral, and steroidal lipids, virosomes, and liposomes), antibodies, lectins, ligands, sugars, steroids, hormones, nutrients, and proteins can serve as targeting moieties" (See page 9, paragraph 4). The instant invention is distinguishable from the Papahadjopoulos reference as it does not teach that nucleic acids may be a targeting moiety. Therefore, the instant claimed invention is not anticipated by the Papahadjopoulos reference. Applicants respectfully request reconsideration and withdrawal of the present rejection.

## CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims now pending are in condition for allowance, and notification of such is respectfully requested.

No fee is believed to be due in connection with the filing of this Amendment and Response. The Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to Deposit Account Number **06-1448, Reference MGA- 003.01**.

If, for any reason, a telephonic conference with the Applicants would be helpful in expediting prosecution of the instant application, the Examiner is invited to call Applicants' Agent at the telephone number provided below.

Respectfully submitted,

FOLEY HOAG LLP



Jennifer A. Zaruskie, PhD

Reg. No. 50,558

Agent for Applicants

November 12, 2003

Patent Group  
Foley Hoag LLP  
155 Seaport Boulevard  
Boston, MA 02210

Telephone: (617) 832-1000  
Facsimile: (617) 832-7000